# 201-14907

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12/16/03 02:31 PM

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cc:
Subject: Thioesters: TDPN

----- Forwarded by Karen Hoffman/DC/USEPA/US on 12/16/03 02:30 PM -----

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Subject: Thioesters: TDPN

Attached is a submission on behalf of the Thioesters Association for Thiodipropionitrile, CAS Number 111-97-7, under the US HPV Program.

This submission includes the following attached files:

- Test Plan
- IUCLID Dossier

If you have any difficulty opening these files or have any questions, please contact me.

Elizabeth Hunt
Executive Director
Thioesters Association


TDPNTest PlanNov252003clean.do IUCLID thiodipropionitrile Nov 25 2003.

# TEST PLAN FOR THIODIPROPIONITRILE (CAS NO. 111-97-7)

## OVERVIEW

The Thioesters Association agrees to sponsor thiodipropionitrile (CAS No. 111-97-7) in the U.S. EPA High Production Volume Chemical Program. The sponsors hereby submit a test plan for this substance. It is the intent of the sponsors to use existing data plus additional testing as proposed in the test plan to fulfill the Screening Information Set (SIDS) endpoints.

Table 1. Test Plan Matrix for Thiodipropionitrile (CAS No. 111-97-7)

| **CAS No. 111-97-7** | Information | Estimation | Acceptable | New Testing Required |
|---|---|---|---|---|
| **ENDPOINT** | Y/N | Y/N | Y/N | Y/N |
| **PHYS/CHEM PROPERTIES** | | | | |
| Melting Point | Y | N | Y | N |
| Boiling Point | Y | N | Y | N |
| Vapor Pressure | Y | N | Y | N |
| Partition Coefficient | Y | Y | Y | N |
| Water Solubility | Y | N | Y | N |
| **ENVIRONMENTAL FATE** | | | | |
| Photodegradation | Y | Y | Y | N |
| Stability in Water | Y | N | Y | N |
| Biodegradation | N | N | N | Y |
| Transport between Environmental Compartments (Fugacity) | Y | Y | Y | N |
| **ECOTOXICITY** | | | | |
| Acute Toxicity to Fish | Y | Y | N | NR |
| Acute Toxicity to Aquatic Invertebrates | Y | Y | N | NR |
| Toxicity to Aquatic Plants | Y | Y | N | NR |
| **TOXICOLOGICAL DATA** | | | | |
| Acute Toxicity | Y | N | Y | N |
| Repeated Dose Toxicity | Y | N | N | NR |
| Genetic Toxicity-Mutation | N | N | N | Y |
| Genetic Toxicity-Chromosomal Aberrations | N | N | N | Y |
| Toxicity to Reproduction | N | N | N | NR |
| Developmental Toxicity | N | N | N | NR |
| **OTHER TOXICITY DATA** | | | | |
| Skin Irritation (NR) | Y | N | Y | N |
| Eye Irritation (NR) | Y | N | Y | N |
| Sensitization (NR) | Y | N | Y | N |

Y = yes; N = no; NR = toxicity testing is not required because the material is a closed system intermediate (see Appendix I).

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## 1. Introduction

The Thioesters Association has agreed to supply screening information under the U.S. EPA High Production Volume Chemical Program for thiodipropionitrile. The Thioesters Association consists of the following manufacturers: Cytec Industries, Inc. and the Dow Chemical Company. This plan identifies existing data of adequate quality for this chemical, and outlines the intended testing to be conducted.

## 2. Designation of Test Substance

The test substance presented in this test plan is 3,3'-thiodipropionitrile (CAS No. 111-97-7). Its chemical structure is as follows:

$$NCCH_2CH_2SCH_2CH_2CN$$

This substance has the following synonyms:

Di(2-cyanoethyl)sulfide
Propionitrile, 3,3'-thiodi
Sulfide, bis(2-cyanoethyl)
Thiodipropionitrile

## 3. Criteria for Determining Adequacy of Data

All available studies were reviewed and assessed for adequacy according to the standards of Klimisch et al. (1997). Studies receiving a Klimisch rating of 1 or 2 were considered to be adequate.

## 4. Discussion of Available Test Information

The thiodipropionitrile test plan matrix (as shown in Table 1) was constructed after a careful evaluation of all existing data (see below). This matrix is arranged by study type (columns) and screening data endpoints (rows), and indicates if data are provided for each end point in the sets of robust summaries.

### 4.1 Chemical and Physical Properties

The results of chemical/physical property testing are shown in Table 2.

#### 4.1.1 Melting Point

A measured melting point of 25 – 29 °C was obtained in a recent study conducted according to OECD Test Guideline 102 (Cuthbert and Mullee, 2003). A melting point of 25ºC is reported by the Cytec Industries, Inc. material safety data sheet. The results are consistent with the physical state of the product at room temperature. The product is in the form of a solid or liquid, or is

Table 2. Chemical/physical properties of thiodipropionitrile

| **Endpoint** | Thiodipropionitrile (CAS No. 111-97-7) |
|---|---|
| Molecular weight grams/mol | 140.20 |
| Melting point | 25 – 29 °C[a] |
| Boiling point | 163-4 °C at 1 hPa[a] |
| Relative density | 1.11[a] |
| Vapor pressure | 7.3 x 10E-5 hPa[a] at 25° C |
| Partition coefficient (Log Pow or Kow) | -0.05 [b] |
| Water solubility (mg/l at 30 ° C) | 25,000 [a] |

[a]measured; [b] estimated by EPIWIN

partially solid at ambient temperatures (20-30°C), depending on whether the purity is 96.5% or closer to 99%.

### 4.1.2 Boiling Point

A measured boiling point of 163-4 °C at 1 hPa has been reported in the Dow Chemical Company material safety data sheet for thiodipropionitrile.

### 4.1.3 Vapor Pressure

A vapor pressure of 7.3 x $10^{-5}$ hPa at 25° C has been measured using OECD Test Guideline 104 (Tremain, 2003). The EPIWIN-calculated value is 0.03 hPa at 25° C. Measured inputs to the model were a melting point of 27 ° C, boiling point of 250 ° C at 1013 hPa, vapor pressure of 5.5 E-5 mm Hg, and a water solubility of 25,000 mg/l.

### 4.1.4 Octanol/Water Partition Coefficient

The EPIWIN Kowwin program provides a calculated partition coefficient of log Kow = –0.05. Measured inputs to the model were a melting point of 27° C, boiling point of 250 ° C at 1013 hPa, vapor pressure of 5.5 E-5 mm Hg, and a water solubility of 25,000 mg/l.

### 4.1.5 Water Solubility

A measured water solubility value of 25,000 mg/l at 30°C has been reported in the Cytec Industries, Inc. material safety data sheet for thiodipropionitrile. The EPIWIN Wskow program calculates a water solubility of 117,900 mg/l at 25°C.

### 4.1.6 Summary/Test Plan for Physical Properties

Measured values are available for melting point, boiling point, vapor pressure and water solubility. These values are considered to be sufficient to characterize these endpoints. A

calculated value is available for the partition coefficient, using EPIWIN Kowwin. This value is deemed to be adequate to characterize this endpoint.

### 4.2 Environmental Fate/Pathways

Results of environmental fate modeling and studies are summarized in Table 3.

Table 3. Environmental fate parameters for thiodipropionitrile

| Endpoint | Value |
|---|---|
| Indirect Photolysis (OH sensitizer)<br>(Hydroxyl Radical Rate Constant)[b]<br>(Atmospheric $T_{1/2}$) [b] | <br>3.885 E-12 cm3/(molecule*sec)<br>33 hours |
| Stability in Water[a] | $T_{1/2}$ > 1 year at 25 º C |
| Henry's Law Constant[b] | 2.38 E-10 atm-$m^3$/mol |
| Koc[b] | 177.1 |
| Environmental transport<br>(Fugacity Level III mass percentages)[b] | Air = 0.007<br>Water = 49.3<br>Soil = 50.6<br>Sediment = 0.0917 |
| Biodegradation | No measured data, EPIWIN predicts ultimate biodegradation of weeks-months based on the molecular structure |

[a]measured; [b] Estimated using EPIWIN

#### 4.2.1 Photodegradation

Photodegradation with hydroxyl radical sensitizer was estimated using EPIWIN/Aop (v1.90). An overall OH rate constant of 3.885 E-12 $cm^3$/(molecule*sec) was calculated based on the summation of individual rate constants for each bond fragment in the molecule using the program algorithm. A half-life of 33 hours was calculated assuming a constant concentration of OH radical and pseudo first order kinetics.

#### 4.2.2 Stability in Water

According to a recent study conducted according to OECD Test Guideline 111 (Cuthbert and Mullee, 2003), less than 10% of the material hydrolyzes over 5 days in solutions maintained at pH values of 4, 7 and 9 and a temperature of 50 +/- 5 degrees C, and at a physiologically relevant pH and temperature (1.4 and 37 degrees C, respectively). The half-life calculated from the data at pH 4, 7 and 9 was > 1 year at 25 degrees C. However, according to manufacturing information (see Appendix I), hydrolysis of thiodipropionitrile to the corresponding acid salt has been observed at temperatures higher than those used for manufacture (28 - 30ºC).

#### 4.2.3 Fugacity

Level III fugacity modeling has been conducted on the test material using the EPIWIN model. Measured inputs to the program are the melting point, boiling point, and water solubility listed in

Table 2. Emission rates inputted into the program were air: 0 kg/hr, water: 1000 kg/hr, soil: 1000 kg/hr and sediment: 0 kg/hour. The following half-lives were calculated: T ½air = 66 hr, water = 900 hr, soil = 900 hr, and sediment = 3600 hr. The Biowin ultimate value range was weeks to months. A Henry's Law Constant of 2.38 E -10 atm-$m^3$/mol and a soil sediment partition constant (Koc) of 177.1 were estimated using the EPIWIN/Henry and Pckoc Programs, respectively. The percent mass balances predicted for thiodipropionitrile in air, water, soil and sediment are shown in Table 3. The results indicate that the material will partition to water and soil.

### 4.2.4 Biodegradation

A study that provides data on the rate and extent of biodegradation of thoidipropionitrile in the aqueous environment is not available. Biodegradation testing is therefore proposed by the sponsors.

### 4.2.5 Summary/Test Plan for Environmental Fate Parameters

Estimated values are available for the hydroxyl radical induced photolysis rate constant and atmospheric half-life, Henry's Law Constant, soil sediment partition coefficient, and Fugacity Level III environmental transport parameters. No further testing is planned for these endpoints. Biodegradation testing has not been conducted. Since results of the hydrolysis study indicate that the material is fairly stable in water, biodegradation testing is relevant, and will be conducted.

## 4.3 Ecotoxicity

### 4.3.1 Acute Toxicity to Fish

The 96-hr LC50 value for fish estimated by the EPA's ECOSAR neutral organics model is 8785.377 mg/l. No measured data are available.

### 4.3.2 Acute Toxicity to Aquatic Invertebrates

The EPA's ECOSAR neutral organics model predicts a 48-hour EC50 value of 8170.722 mg/l for Daphnia. No measured data are available.

### 4.3.3 Acute Toxicity to Aquatic Plants

The 96 hr EC50 value calculated for green algae by the ECOSAR neutral organics model is 4539.524 mg/l. No measured data are available.

### 4.3.4 Summary/Test Plan for Ecotoxicity

LC50 and EC50 toxicity values have been estimated by EPIWIN ECOSAR for fish, Daphnia and green algae. The values for all three species are > 4539 mg/l, which suggests that the material is of low toxicity to these species. Since the material is a site limited, wholly consumed Type A intermediate (see Appendix I), waste streams contain only minimal concentrations of thiodipropionitrile. Therefore, environmental concentrations will be considerably less than those

estimated by ECOSAR to be toxic to aquatic species. For this reason, no aquatic toxicity testing is planned.

## 4.4 Human Health Data

### 4.4.1 Acute Mammalian Toxicity

This endpoint is filled by sufficient oral, inhalation and dermal toxicity studies in rodents. The $LD_{50}$ value for the oral study in mice conducted with thiodipropionitrile of > 90% purity is 3.75 g/kg (Tusing, 1953a). Inhalation exposure to a saturated vapor of thiodipropionitrile (containing approximately> 15.5 ppm) for 6 hours did not cause death or signs of toxicity in rats, mice or guinea pigs (Tusing, 1953b). The dermal $LD_{50}$ value in guinea pigs was > 8 ml/kg (8.876 g/kg) (Tusing, 1953a).

Signs of toxicity in mice orally exposed to lethal concentrations included squinting, lacrimation, rapid and labored respiration, ataxia and depression, vasodilation around the mouth, mild clonic convulsions and coma preceding death. Postmortem examinations of mice that died revealed hemorrhagic or hyperemic lungs, distended stomachs, irritated intestines (with vasodilation in some cases), mottled livers and granular kidneys. In addition, blood clots were observed in the region of the transverse sinuses of 2 mice treated with 4.4 g/kg. No other brain damage was observed grossly. Animals that survived until necropsy had normal gross pathology.

### 4.4.2 Repeated Dose Mammalian Toxicity

Two repeated dose toxicity experiments have been performed with thiodipropionitrile.

Results of a 10-day repeated dose dermal study in rabbits show that application of 1.0 g/kg/day did not cause toxicity in 5/6 animals (Tusing, 1953a). After 6 treatments, one animal developed an apparent weakness or incoordination of the hind extremities. This behavior persisted until study termination. Placement and righting reflexes in this animal were normal. This animal also developed diarrhea, weight loss, and an "unthrifty" appearance. There were no significant necropsy findings in any of the animals (including the animal with diarrhea).

Rats have been given 100, 1,000 and 10,000 ppm thiodipropionitrile in the diet for 32 continuous days (Tusing, 1953b). Based on the average amount of food consumed and average body weights, the amount of test material consumed on a mg/kg/day basis was 10.7, 104.8 and 1010.8 for the 100, 1,000 and 10,000 ppm groups, respectively. In this study, the authors concluded that there was no evidence of toxicity at any dose level. However, one animal exposed to 100 and another to10,000 ppm died during the study. In addition, gross pathological changes in the liver and kidneys were observed in animals treated with 1,000 and 10,000 ppm. Since this study was not conducted according to current standards, it was given a reliability rating of 4 (not assignable).

Although these studies are not up to current standards, no further repeat dose testing is required, since the substance is a Type A industrial intermediate (see Appendix I).

### 4.4.3 Genetic Toxicity

#### 4.4.3.1 Mutagenicity

Mutagenicity testing has not been conducted. Testing is proposed for this endpoint.

#### 4.4.3.2 Chromosomal aberration

No tests for this endpoint were located. Testing is proposed for this endpoint.

### 4.4.4 Reproductive and Developmental Toxicity

Reproductive or developmental toxicity tests with thiodipropionitrile have not been performed. Thiodipropionitrile is used exclusively as a closed-system (Type A) industrial intermediate, chemically converted to other products. The potential for significant human exposure is strictly limited. Therefore it is believed that this material qualifies for exemption from reproductive toxicity testing under the established guidelines of the U.S. EPA HPV chemical program. Detailed documentation of the information required to substantiate manufacture and use as a closed-system industrial intermediate with limited exposure is provided in Appendix I of this test plan.

According to the U.S. EPA HPV Chemical program for Type A intermediates, developmental toxicity testing is required. However, due to the precautions involved in use and manufacture of the material (see Appendix I), the possibility for exposure is extremely low. Therefore, we believe that developmental toxicity testing is not necessary.

### 4.4.5 Additional Data

#### 4.4.5.1 Skin and Eye Irritation

The results of a repeated dose dermal toxicity study in rabbits with material of fairly high purity (> 90%) indicate that 1.0 ml/kg thiodipropionitrile is not irritating to skin (Tusing, 1953b). In an acute study, application of 4.0 ml/kg (but not 8.0 ml/kg) to rabbits caused behavior indicative of burning or pain (Tusing, 1953a). Application of undiluted material to rabbit eyes caused pain, vascularization of the sclera and nictitating membrane and some edema of the upper eyelid that resolved within an hour.

#### 4.4.5.2 Sensitization

The ability of thiodipropionitrile to produce sensitization was tested in modified repeated dose dermal toxicity study in rabbits (Tusing, 1953b). Test material (1.0 ml/kg) was applied dermally 5 days/week for a total of 10 applications, and a challenge dose of 1.0 m/kg was applied after a 10 day rest period. None of the rabbits tested exhibited any evidence of sensitization over the next 5 days.

### 4.4.6 Summary/Test Plan for Mammalian Toxicity

Adequate acute toxicity studies have been conducted for thidiopropionitrile. Results of these studies show that exposure to fairly large amounts of thiodipropionitrile is required to produce acute toxicity. The material may cause irritation to the skin and eyes immediately after exposure, which quickly resolves.

Results of repeated dose oral and dermal toxicity studies show that fairly high doses of thiodipropionitrile are required to produce toxicity. However, microscopic analyses and laboratory tests that are currently required of repeated dose toxicity studies were not performed. Although these studies are not up to current standards, no further repeat dose testing is proposed, since the substance is a Type A industrial intermediate. No reproductive or developmental toxicity data are available, but no testing is planned for these endpoints, since the substance is a Type A industrial intermediate with extremely low probability of exposure (see Appendix I). No data are available for mutagenicity or, chromosomal aberrations, so this testing is planned.

## 5. Summary

Physical properties

Adequate data exist to characterize melting point, boiling point, water solubility and partition coefficient. A value for the partition coefficient (log Kow) has been estimated using the EPIWIN KOWWIN program. No physical property testing is proposed.

Environmental fate properties

EPIWIN modeling provides adequate data for hydroxyl radical induced atmospheric photodegradation and environmental transport, as well as bioconcentration factor and Henry's Law Constant. Thiodipropionitrile is known to have limited stability in water and hydrolyses to the corresponding thiodipropionic acid (CAS No. 111-17-1) or its salt, depending on pH and temperature. Measured data indicate that hydrolysis occurs slowly at ambient temperatures. As mentioned earlier, no biodegradation data are available and a biodegradation study is proposed.

Aquatic toxicity

Testing in fish, Daphnia or algae has not been performed. $LC/EC_{50}$ values for thiodipropionitrile in these species have been estimated using ECOSAR. Acute aquatic testing is not proposed for fish, daphnia and algae, since the $LC/EC_{50}$ values predicted by ECOSAR are substantially higher than expected environmental concentrations (See Appendix I for further documentation).

Mammalian toxicity

Adequate acute mammalian toxicity data are available, and no testing is proposed for this endpoint. No data are available for mutagenicity or chromosomal aberrations; therefore testing to fill these endpoints is proposed. No reproductive or developmental toxicity studies are available, but no testing is proposed, because thiodipropionitrile is manufactured and used exclusively as a site limited, closed system (Type A) industrial intermediate and extra precautions are taken to limit exposure (See Appendix I for further documentation). Repeat dose studies are available and summarized. Although these studies are not up to current standards, no further repeat dose testing is required, since the substance is a Type A industrial intermediate.

## 6. References

American Cyanamid Company. 1953. Data sheet for toxicity study.

Cuthbert JE and Mullee DM. 2003. 3,3'-thiodipropionitrile (CT-781-03): Determination of melting point/melting range and hydrolysis as a function of pH. SafePharm Laboratories (SPL) project number 971/210, dated September 24, 2003 (unpublished).

Cytec Industries Inc. 1997. Material safety data sheet for thiodipropionitrile, dated July 1.

EPIWIN AOP (v1.90).

EPIWIN BCF (v2.14)

EPIWIN ECOSAR (v0.99g)

EPIWIN HENRY (v3.10)

EPIWIN HYDROWIN (v1.67).

EPIWIN KOWWIN (v1.66).

EPIWIN Level III Fugacity modeling program.

EPIWIN MPBPWIN (v1.40).

EPIWIN PCKOC Program (v1.66).

EPIWIN WSKOW (v1.40).

Fieser, L and Fieser, M, Advanced Organic Chemistry, pp 365-6 (1961).

Klimisch HJ, Andreae M and Tillmann U. 1997. A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Reg Tox Pharm 25:1-5.

The Dow Chemical Company. 2001. Material safety data sheet for thiodipropionitrile, dated December 3.

Tremain SP. 2003. 3,3'-thiodipropionitrile (CT-781-03): Determination of vapour pressure. SafePharm Laboratories (SPL) project number 971/211, dated September 24, 2003 (unpublished).

Tusing TW. 1953a. Progress Report : B,B' Thiodipropionitrile Acute Oral and Dermal Toxicity and Acute Eye Irritation. Hazleton Laboratories Report to American Cyanamid Company, dated Feb. 24, 1953 (unpublished).

Tusing TW. 1953b. Progress Report : B,B' Thiodipropionitrile Repeated Dermal Application, Acute Inhalation Toxicity, and Subacute Feeding. Hazleton Laboratories Report to American Cyanamid Company, dated March 30, 1953 (unpublished).

## APPENDIX I

**Documentation of manufacture and use of thiodipropionitrile as an industrial intermediate**

According to the EPA Guidance for Testing Closed System Intermediates for the HPV Challenge Program, "any chemical which is intended to undergo a further deliberate reaction to produce another industrial substance is considered an intermediate."

It is believed that thiodipropionitrile is a closed system intermediate that fits the description of a Type A closed system industrial intermediate. This description is as follows:

(a) isolated intermediates which are stored in controlled on-site facilities

The EPA guidance also states that documentation is to be provided to support the claim for reduced testing. Such documentation includes information on number of sites, basis for closed process, and information on release, transportation or presence in distributed product. This information for thiodipropionitrile is provided below:

Thiodipropionitrile is manufactured at two plant sites in the United States. These sites are owned and operated by Cytec Industries Inc. and The Dow Chemical Company (one site per company). At each site, manufacture is carried out in a closed system by the reaction of acrylonitrile with sodium sulfhydrate (SSH) in an aqueous medium. The total number of workers involved in the manufacture and use processes at the two plant sites is approximately 40 for Dow and 8 for Cytec Industries Inc. The reactants are each added to the reactor from closed feed tanks through closed lines. A slight molar excess of SSH is employed to assure complete chemical conversion of acrylonitrile. The reaction temperature is maintained between 28-30°C, since thiodipropionitrile undergoes significant hydrolysis to thiodipropionic acid and its sodium salt at higher temperatures.

The product liquid thiodipropionitrile layer is purified by water washing and separation within the closed reactor, and transported through closed lines to a storage tank. From the storage tank, thiodipropionitrile is transferred on site through closed lines to another reactor for conversion to a different chemical used to manufacture thio chemicals. In addition to the liquid product layer, the reaction process has three other process layers, which are the aqueous alkaline layer containing excess SSH, and two water washes. The water washes are recycled to the process and any waste aqueous layers are sent to plant waste process water treatment facilities for biodegradation. These streams contain minimal concentrations of thiodipropionitrile. The major organic component of these streams is byproduct waste, thiodipropionic acid, sodium salt, which is formed by hydrolysis of the product.

At both Cytec Industries Inc. and the Dow Chemical Company the sole use of thiodipropionitrile is as a closed system industrial intermediate, which is completely converted to other thio chemicals at the same plant site. There are no sales of thiodipropionitrile, the intermediate does

not leave the manufacturing site at either company, and thiodipropionitrile is not present appreciably in any downstream product.

Although no industrial hygiene monitoring data are available for thiodipropionitrile at either manufacturing facility, the closed system manufacturing and conversion processes, coupled with the limited volatility and high boiling point (163-4°C at 1 hPa) of thiodipropionitrile both suggest that any worker exposure to this substance would be infrequent and at a very low level. Extra precautions must be taken (closed system, engineering controls, personal protective clothing as appropriate, etc.) to comply with special, strict Occupational Safety and Health Administration (OSHA) regulations (29 CFR 1910.1045) designed to prevent exposure to acrylonitrile, the raw material used to manufacture TDPN. These regulations have been in place since 1980. The current OSHA TLV for acrylonitrile is 2 ppm. As required by the OSHA regulations, whenever the concentration of acrylonitrile is unknown, a supplied air and auxiliary self-contained breathing apparatus with full facepiece in positive pressure mode is required to minimize exposure to acrylonitrile vapor. In addition, impermeable protective clothing is used to protect any area of the body which may come in contact with liquid acrylonitrile. During maintenance in these plants, workers are required to wear a complete suit to minimize exposure to acrylonitrile. In addition, all employees exposed to acrylonitrile at concentrations at or above the action level of 1 ppm are required to be part of a medical surveillance program. The protective equipment worn to reduce/eliminate exposure to acrylonitrile, a more volatile material, should minimize worker exposure to thiodipropionitrile.
Protective equipment includes impervious gloves and an apron to prevent skin contact, chemical splash-proof goggles or a face shield, and a NIOSH approved respirator when there is potential for inhalation exposure (Cytec Industries Inc., 1997).

201-14907

# I U C L I D

# Data Set



| | | |
|---|---|---|
| **Existing Chemical** | : | ID: 111-97-7 |
| **CAS No.** | : | 111-97-7 |
| **Producer related part** | | |
| **Company** | : | The Thioesters Association |
| **Creation date** | : | 30.04.2003 |
| **Substance related part** | | |
| **Company** | : | The Thioesters Association |
| **Creation date** | : | 30.04.2003 |
| **Status** | : | |
| **Memo** | : | |
| **Printing date** | : | 25.11.2003 |
| **Revision date** | : | 25.11.2003 |
| **Date of last update** | : | 25.11.2003 |
| **Number of pages** | : | 27 |
| **Chapter (profile)** | : | Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10 |
| **Reliability (profile)** | : | Reliability: without reliability, 1, 2, 3, 4 |
| **Flags (profile)** | : | Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS |

### 1.0.1 APPLICANT AND COMPANY INFORMATION

### 1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

### 1.0.3 IDENTITY OF RECIPIENTS

### 1.0.4 DETAILS ON CATEGORY/TEMPLATE

### 1.1.0 SUBSTANCE IDENTIFICATION

### 1.1.1 GENERAL SUBSTANCE INFORMATION

**Purity type** :
**Substance type** : organic
**Physical status** : solid
**Purity** : = 96.5 % w/w
**Colour** :
**Odour** :

**Reliability** : (2) valid with restrictions

(2)

**Purity type** :
**Substance type** : organic
**Physical status** : solid
**Purity** : > 99 % w/w
**Colour** :
**Odour** :

**Remark** : Since the melting point is about 25-29 degrees C, the substance may be a liquid, or only partially solid at ambient temperature.
**Reliability** : (2) valid with restrictions

(10)

### 1.1.2 SPECTRA

### 1.2 SYNONYMS AND TRADENAMES

**3,3'-Thiodipropionitrile**

(9)

**Propionitrile, 3,3'-thiodi**

(9)

**Sulfide, bis(2-cyanoethyl)**

(9)

**Thiodipropionitrile**

(9)

## 1.3 IMPURITIES

**Purity** :
**CAS-No** : 111-17-1
**EC-No** : 203-841-3
**EINECS-Name** : 3,3'-thiodi(propionic acid)
**Molecular formula** :
**Value** : <= 1 % w/w

**Reliability** : (2) valid with restrictions

(10)

**Purity** :
**CAS-No** : 107-96-0
**EC-No** : 203-537-0
**EINECS-Name** : 3-mercaptopropionic acid
**Molecular formula** :
**Value** : <= 1 % w/w

**Reliability** : (2) valid with restrictions

(10)

**Purity** :
**CAS-No** : 1119-62-6
**EC-No** : 214-284-0
**EINECS-Name** : 3,3'-dithiobispropionic acid
**Molecular formula** :
**Value** : <= 1 % w/w

**Reliability** : (2) valid with restrictions

(10)

**Purity** :
**CAS-No** : 7732-18-5
**EC-No** : 231-791-2
**EINECS-Name** : Water
**Molecular formula** :
**Value** : <= 3.5 % w/w

**Reliability** : (2) valid with restrictions

(10)

**Purity** :
**CAS-No** : 107-13-1
**EC-No** : 203-466-5
**EINECS-Name** : acrylonitrile
**Molecular formula** :
**Value** : <= 1 % w/w

**Reliability** : (2) valid with restrictions

(10)

**Purity** :
**CAS-No** :

| | | |
|---|---|---|
| **EC-No** | : | |
| **EINECS-Name** | : | dithiopropionitrile |
| **Molecular formula** | : | |
| **Value** | : | <= 1 % w/w |
| **Reliability** | : | (2) valid with restrictions |

(10)

| | | |
|---|---|---|
| **Purity** | : | |
| **CAS-No** | : | |
| **EC-No** | : | |
| **EINECS-Name** | : | mercaptopropionitrile |
| **Molecular formula** | : | |
| **Value** | : | <= 1 % w/w |
| **Reliability** | : | (2) valid with restrictions |

(10)

## 1.4 ADDITIVES

| | | |
|---|---|---|
| **Remark** | : | No intentional additives per the reference. |
| **Reliability** | : | (1) valid without restriction |

(10)

## 1.5 TOTAL QUANTITY

## 1.6.1 LABELLING

## 1.6.2 CLASSIFICATION

## 1.6.3 PACKAGING

## 1.7 USE PATTERN

| | | |
|---|---|---|
| **Type of use** | : | industrial |
| **Category** | : | Chemical industry: used in synthesis |
| **Remark** | : | According to the manufacturers, Cytec Industries, Inc. and The Dow Chemical Company, thiodipropionitrile is used solely as a closed system industrial intermediate that is site limited. |
| **Source** | : | Cytec Industries, Inc. |
| **Reliability** | : | (2) valid with restrictions |

## 1.7.1 DETAILED USE PATTERN

## 1.7.2 METHODS OF MANUFACTURE

## 1.8 REGULATORY MEASURES

### 1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

**Remark** : No established exposure limit known.
**Reliability** : (2) valid with restrictions

(2)

### 1.8.2 ACCEPTABLE RESIDUES LEVELS

### 1.8.3 WATER POLLUTION

### 1.8.4 MAJOR ACCIDENT HAZARDS

### 1.8.5 AIR POLLUTION

### 1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

### 1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

### 1.9.2 COMPONENTS

## 1.10 SOURCE OF EXPOSURE

## 1.11 ADDITIONAL REMARKS

## 1.12 LAST LITERATURE SEARCH

## 1.13 REVIEWS

## 2.1 MELTING POINT

| | | |
|---|---|---|
| **Value** | : | = 25 - 29 °C |
| **Sublimation** | : | |
| **Method** | : | OECD Guideline 102 |
| **Year** | : | 2003 |
| **GLP** | : | yes |
| **Test substance** | : | as prescribed by 1.1 - 1.4 |
| **Result** | : | In both studies, the melting point range was 298 to 302 +/- 0.5 degrees K. There was approximately 1 degree K difference in the onset of melting (meniscus formation) for the two determinations (298 and 299 degrees K, respectively). It was completely melted (a clear liquid) at 302 degrees K in both studies . The test material was a white solid at 294 degrees K in the first study, and 292 degrees K in the second. |
| **Test condition** | : | A fused capillary tube (80 – 100 mm long, 1.0 +/- 0.2 mm diameter) was filled with test material to a level of 3 mm. The filled tube was then placed in a freezer to solidify the material. The capillary tube was inserted into a liquid bath containing ice, water and acetone through a side port in the melting point apparatus. Two thermometers were inserted at the top of the apparatus through a 2 -hole stopper. One (thermometer 1) was inserted down into the bath and the other (thermometer 2) was positioned above the bath, at the level of mercury in the other thermometer. Thermometer 2 measured the temperature of the atmosphere at the emergent stem The end of the capillary tube was positioned against the bulb of thermometer 1. The bath was heated with an electric heating mantle at a rate of 1 degree K/min. The bath was stirred constantly with a magnetic stir bar. Temperatures of the bath and atmosphere were recorded, along with any observations about the appearance of the test material. The procedure was performed in duplicate.<br><br>The temperature readings were corrected using the following equation:<br><br>Corrected temperature (K) = temperature of the bath (K) + 0.00016 x [temperature of the bath – temperature of the emergent stem (from thermometer 2)] x number of gradations of mercury thread of thermometer 1 at the emergent stem. |
| **Test substance** | : | Purity of the test material was not determined in the study. It was used as supplied by Cytec Industries, Inc. It is assumed that it was of the same purity as material described in the current MSDS (96.5%). |
| **Reliability** | : | (1) valid without restriction<br>Test was conducted according to an established guideline. |
| **Flag** | : | Critical study for SIDS endpoint |

(1)

| | | |
|---|---|---|
| **Value** | : | = 25 °C |
| **Sublimation** | : | |
| **Method** | : | other |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | as prescribed by 1.1 - 1.4 |
| **Remark** | : | No details for method of melting point determination, however this melting point value is in good agreement with the 25 - 29 degrees C value reported above. |
| **Reliability** | : | (2) valid with restrictions |

Data came from a MSDS.

**Flag** : Material Safety Dataset

(2)

### 2.2 BOILING POINT

**Value** : = 163 - 164 °C at
**Decomposition** :
**Method** : other
**Year** :
**GLP** : no data
**Test substance** : as prescribed by 1.1 - 1.4

**Reliability** : (2) valid with restrictions
Experimental details were not provided. Data came from a MSDS.
**Flag** : Critical study for SIDS endpoint

(10)

### 2.3 DENSITY

**Type** : relative density
**Value** : = 1.11 at °C
**Method** : other
**Year** :
**GLP** : no data
**Test substance** : as prescribed by 1.1 - 1.4

**Reliability** : (2) valid with restrictions
Experimental details were not provided.
**Flag** : Material Safety Dataset

(2)

### 2.3.1 GRANULOMETRY

### 2.4 VAPOUR PRESSURE

**Value** : = 7.3 x 10 E-5 hPa at 25 °C
**Decomposition** :
**Method** : OECD Guideline 104
**Year** : 2003
**GLP** : yes
**Test substance** : as prescribed by 1.1 - 1.4

**Result** : The equations fit to the log10Vp (Pa) vs. 1/temperature (degrees K) for the six runs were as follows: (1) log10Vp (Pa) = -4093.322/temp (K) + 11.597; (2) log10Vp (Pa) = -4201.011/temp (K) + 11.922; (3) log10Vp (Pa) = -4104.380/temp (K) + 11.364; (4) log10Vp (Pa) = -4009.591/temp (K) + 11.343; (5) log10Vp (Pa) = -4329.233/temp (K) + 12.302; (6) log10Vp (Pa) = -3827.006/temp (K) + 10.781. The corresponding log10Vp (Pa) values at 298.15 degrees K (25 degrees C) were -2.132, -2.168, -2.133, -2.105, -2.219, and -2.054. The average log10Vp (Pa) of -2.135 is equal to a vapor pressure of 7.3 E-3 Pa.

**Test condition** : The vapor pressure was determined using a vapor pressure balance. After evacuating the system, opening the shutter above the sample oven caused

the escaping vapor jet to be directed at the scale pan. The difference in mass readings with the orifice covered and uncovered is proportional to the vapor pressure at the oven temperature. The temperature of the sample was controlled electronically. The mass and temperature readings were recorded automatically into a computer file.

A sequence of 6 runs was started after a sample of test material had been under vacuum for approximately 6 hours. Temperature and pressure readings were taken between 52 and 62 degrees C with a one hour period at 52 degrees C between runs.

The vapor pressure (Vp) was calculated according to the following equation:

Vp (Pa) = mass difference (kg) x 9.813 m/s E-2 (acceleration due to gravity) / 7.06858 x 10E-6 mE2 (area of the orifice).

A plot of log10 Vp (Pa) versus the reciprocal temperature (degrees K) was made, which resulted in a straight line gr aph. The vapor pressure at 298.15 degrees K was extrapolated from the graph.

**Test substance** : Purity of the test material was not determined in the study. It was used as supplied by Cytec Industries, Inc. It is assumed that it was of the same purity as material described in the current MSDS (96.5%).

**Reliability** : (1) valid without restriction
Test was conducted according to an established guideline.

**Flag** : Critical study for SIDS endpoint

(11)

**Value** : = .03 hPa at 25 °C
**Decomposition** :
**Method** : other (calculated)
**Year** : 2003
**GLP** : No
**Test substance** : as prescribed by 1.1 - 1.4

**Remark** : Measured inputs to the model are melting point (27 degrees C), boiling point (163-164 degrees C at 1 mm Hg extrapolated to 250 degrees C at 1013 hPa), and water solubility (25,000 mg/l at 30 degrees C).

**Reliability** : (2) valid with restrictions
Data were obtained by modeling.

**Flag** : Critical study for SIDS endpoint

(7)

## 2.5 PARTITION COEFFICIENT

**Partition coefficient** :
**Log pow** : = -.05 at 20 °C
**pH value** :
**Method** : other (calculated)
**Year** : 2003
**GLP** : no
**Test substance** : as prescribed by 1.1 - 1.4

**Remark** : Measured inputs to the model are melting point (27 degrees C), boiling point (163-164 degrees C at 1 mm Hg extrapolated to 250 degrees C at 1013 hPa), vapor pressure (5.5 E-5 mm Hg), and water solubility (25,000 mg/l at 30 degrees C).

**Reliability** : (2) valid with restrictions

Data were obtained by modeling.

**Flag** : Critical study for SIDS endpoint

(6)

### 2.6.1 SOLUBILITY IN DIFFERENT MEDIA

**Solubility in** : water
**Value** : ca. 25000 mg/l at 30 °C
**pH value** :
**concentration** : at °C
**Temperature effects** :
**Examine different pol.** :
**pKa** : at 25 °C
**Description** :
**Stable** :
**Deg. product** :
**Method** : other
**Year** :
**GLP** : no data
**Test substance** : as prescribed by 1.1 - 1.4

**Reliability** : (2) valid with restrictions
No experimental details were given. Data came from a MSDS.
**Flag** : Critical study for SIDS endpoint

(2)

**Solubility in** : water
**Value** : ca. 117,900 mg/l at 25 °C
**pH value** :
**concentration** : at °C
**Temperature effects** :
**Examine different pol.** :
**pKa** : at 25 °C
**Description** :
**Stable** :
**Deg. product** :
**Method** : other: calculated using EPIWIN Wskow (v1.40)
**Year** : 2003
**GLP** : no
**Test substance** : as prescribed by 1.1 - 1.4

**Remark** : Measured inputs to the model are melting point (27 degrees C), boiling point (163-164 degrees C at 1 mm Hg extrapolated to 250 degrees C at 1013 hPa), vapor pressure (5.5 E-5 mm Hg), and water solubility (25,000 mg/l at 30 degrees C).
**Reliability** : (2) valid with restrictions
Data were obtained by modeling.

(8)

### 2.6.2 SURFACE TENSION

### 2.7 FLASH POINT

**Value** : = 80 °C
**Type** : closed cup
**Method** : other
**Year** :

**GLP** : no data
**Test substance** : as prescribed by 1.1 - 1.4

**Reliability** : (2) valid with restrictions
Experimental details were not provided. Data came from a MSDS.

(2)

## 2.8 AUTO FLAMMABILITY

## 2.9 FLAMMABILITY

## 2.10 EXPLOSIVE PROPERTIES

## 2.11 OXIDIZING PROPERTIES

## 2.12 DISSOCIATION CONSTANT

## 2.13 VISCOSITY

## 2.14 ADDITIONAL REMARKS

### 3.1.1 PHOTODEGRADATION

| | | |
|---|---|---|
| **Type** | : | air |
| **Light source** | : | |
| **Light spectrum** | : | nm |
| **Relative intensity** | : | based on intensity of sunlight |
| **INDIRECT PHOTOLYSIS** | | |
| **Sensitizer** | : | OH |
| **Conc. of sensitizer** | : | |
| **Rate constant** | : | = .000000000003885 $cm^3$/(molecule*sec) |
| **Degradation** | : | = 50 % after 33 hour(s) |
| **Deg. product** | : | |
| **Method** | : | other (calculated) |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | as prescribed by 1.1 - 1.4 |
| **Remark** | : | Measured inputs to the model are melting point (27 degrees C), boiling point (163-164 degrees C at 1 mm Hg extrapolated to 250 degrees C at 1013 hPa), vapor pressure (5.5 E-5 mm Hg), and water solubility (25,000 mg/l at 30 degrees C). |
| **Reliability** | : | (2) valid with restrictions<br>Data were obtained by modeling. |
| **Flag** | : | Critical study for SIDS endpoint |

(3)

### 3.1.2 STABILITY IN WATER

| | | |
|---|---|---|
| **Type** | : | abiotic |
| **t1/2 pH4** | : | > 1 year at 25 degree C |
| **t1/2 pH7** | : | > 1 year at 25 degree C |
| **t1/2 pH9** | : | > 1 year at 25 degree C |
| **Deg. Product** | : | no |
| **Method** | : | OECD Guide-line 111 |
| **Year** | : | 2003 |
| **GLP** | : | yes |
| **Test substance** | : | as prescribed by 1.1 – 1.4 |
| **Result** | : | After incubation for 5 days at 50 degrees C and pH 4, 7 and 9, 91.0%, 98.1% and 99.3% of the material remained, respectively. Less than 10% hydrolysis was observed at all conditions (which corresponded to a half life of > 1 year at 25 degrees C).<br><br>The investigation at pH 1.4 and 37 degrees C was performed to simulate the hydrolysis of the test material in the human stomach. After 5 days at pH 1.4 and 37 degrees C, 97.2% of the initial test material remained. |
| **Test Condition** | : | The buffer solutions were filtered through a 0.2 micrometer membrane to ensure sterility before starting the test. The solutions were subjected to ultrasonication and degassing with nitrogen to minimize dissolved oxygen content, and then (with the exception of the pH 1.2 run) pre-equilibrated to test temperature prior to use. Sample solutions were prepared in stoppered glass flasks at a nominal concentration of 1.0 g/l in the buffer solutions. The solutions were shielded from light while maintained at the test temperature. Initial testing was conducted with sample solutions at pH 4, 7 and 9, maintained at temperatures of 50.0 ± 0.5 degrees C for 5 days. Further testing was undertaken at physiological pH and temperature (1.4 and 37.0 ± |

0.5 degrees C, respectively) for a period of 5 days. Aliquots of the sample solutions were taken from the flasks at various times and the pH of each solution recorded.

The concentration of the sample solution was determined by high performance liquid chromatography (HPLC). Duplicate aliquots of sample solution were diluted by a factor of 10 with water and acetonitrile to give a final matrix of buffer:water:acetonitrile of 10:40:50 (v/v/v). Duplicate standard solutions of test material were prepared in the matrix at a nominal concentration of 100 mg/l.

An aliquot (20 microliters) of each sample solution or standard was injected onto a Develosil RP Aqueous column (250 x 4.6 mm id). The column temperature was 40 degrees C. The mobile phase was acetonitrile/water (25:75 v/v), and the flow rate was 1.0 ml/min. The UV detector wavelength was 205 nm.

The mean peak area of each standard was corrected to a nominal concentration of 100 mg/l and the mean value taken. The concentration of the sample solutions (g/l) was calculated using the following equation:

$$C_{spl} = (P_{spl}/P_{std}) \times C_{std} \times D \times 1/1000$$

where:

$C_{spl}$ = sample concentration (g/l)
$P_{spl}$ = mean peak area (or height) of sample solution
$P_{std}$ = mean peak area of standard solution, corrected to nominal standard concentration
$C_{std}$ = nominal standard concentration (100 mg/l)
D = sample dilution factor (0.04)

The rate constant was not calculated due to the lack of degradation. The method of determining the half-life was not stated.

The linearity of the detector response in respect to concentration was assessed over the nominal concentration range of 0 to 200 mg/l. This was satisfactory, with a correlation coefficient of 1.000 being obtained.

**Test substance** : Purity of the test material was not determined in the study. It was used as supplied by Cytec Industries, Inc. It is assumed that it was of the same purity as material described in the current MSDS (96.5%).

**Conclusion** : The material is stable for 5 days at pH 4, 7 and 9 at 50 degrees C and at pH 1.4 and 37 degrees C.

**Reliability** : (1) valid without restriction
Study was conducted according to an OECD guideline, using GLP.

**Flag** : Critical study for SIDS endpoint.

(1)

### 3.1.3 STABILITY IN SOIL

### 3.2.1 MONITORING DATA

### 3.2.2 FIELD STUDIES

### 3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

| | | |
|---|---|---|
| **Type** | : | fugacity model level III |
| **Media** | : | water – air |
| **Air** | : | 0.00709 % (Fugacity Model Level I) |
| **Water** | : | 49.3 % (Fugacity Model Level I) |
| **Soil** | : | 50.6 % (Fugacity Model Level I) |
| **Biota** | : | 0.0917 % (Fugacity Model Level II/III) |
| **Soil** | : | % (Fugacity Model Level II/III) |
| **Method** | : | other |
| **Year** | : | 2003 |
| **Remark** | : | Measured inputs to the model are melting point (27 degrees C), boiling point (163-164 degrees C at 1 mm Hg extrapolated to 250 degrees C at 1013 hPa), vapor pressure (5.5 E-5 mm Hg), and water solubility (25,000 mg/l at 30 degrees C). Emission rates inputted into the program were air: 0 kg/hr, water: 1000 kg/hr, soil: 1000 kg/hr and sediment: 0 kg/hour. Half-lives in various media are air: 66.07 hours; water: 900 hours; soil: 900 hours; and sediment: 3600 hours. Ultimate biodegradation is estimated roughly at weeks to months. The Henry's Law Constant [calculated by EPIWIN Henry (v3.10)] is 2.38 E-10 atm-m3/mol (bond est.). The soil-sediment coefficient [calculated by EPIWIN PCKOC (v1.66)] is Koc = 177.1. |
| **Reliability** | : | (2) valid with restrictions<br>Data were obtained by modeling. |
| **Flag** | : | Critical study for SIDS endpoint |

(5)

### 3.3.2 DISTRIBUTION

### 3.4 MODE OF DEGRADATION IN ACTUAL USE

### 3.5 BIODEGRADATION

### 3.6 BOD5, COD OR BOD5/COD RATIO

### 3.7 BIOACCUMULATION

### 3.8 ADDITIONAL REMARKS

## 4.1 ACUTE/PROLONGED TOXICITY TO FISH

| | | |
|---|---|---|
| **Type** | : | other |
| **Species** | : | |
| **Exposure period** | : | 96 hour(s) |
| **Unit** | : | mg/l |
| **LC50** | : | = 8785.377 calculated |
| **Method** | : | other |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | as prescribed by 1.1 - 1.4 |
| **Remark** | : | Measured inputs to the model are melting point (27 degrees C), boiling point (163-164 degrees C at 1 mm Hg extrapolated to 250 degrees C at 1013 hPa), vapor pressure (5.5 E-5 mm Hg), and water solubility (25,000 mg/l at 30 degrees C). The EPIWIN ECOSAR model used was neutral organic compound. |
| **Reliability** | : | (2) valid with restrictions<br>Data were obtained by modeling. |
| **Flag** | : | Critical study for SIDS endpoint |

(4)

## 4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

| | | |
|---|---|---|
| **Type** | : | other |
| **Species** | : | Daphnia magna (Crustacea) |
| **Exposure period** | : | 48 hour(s) |
| **Unit** | : | mg/l |
| **EC50** | : | = 8170.722 calculated |
| **Method** | : | other |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | as prescribed by 1.1 - 1.4 |
| **Remark** | : | Measured inputs to the model are melting point (27 degrees C), boiling point (163-164 degrees C at 1 mm Hg extrapolated to 250 degrees C at 1013 hPa), vapor pressure (5.5 E-5 mm Hg), and water solubility (25,000 mg/l at 30 degrees C). The EPIWIN ECOSAR model used was neutral organic compound. |
| **Reliability** | : | (2) valid with restrictions<br>Data were obtained by modeling. |
| **Flag** | : | Critical study for SIDS endpoint |

(4)

## 4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

| | | |
|---|---|---|
| **Species** | : | other algae: green algae |
| **Endpoint** | : | biomass |
| **Exposure period** | : | 96 hour(s) |
| **Unit** | : | mg/l |
| **EC50** | : | = 4539.524 calculated |
| **Method** | : | other |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | as prescribed by 1.1 - 1.4 |

| | | |
|---|---|---|
| **Remark** | : | Measured inputs to the model are melting point (27 degrees C), boiling point (163-164 degrees C at 1 mm Hg extrapolated to 250 degrees C at 1013 hPa), vapor pressure (5.5 E-5 mm Hg), and water solubility (25,000 mg/l at 30 degrees C ). The EPIWIN ECOSAR model used was neutral organic compound. |
| **Reliability** | : | (2) valid with restrictions<br>Data were obtained by modeling. |
| **Flag** | : | Critical study for SIDS endpoint |

(4)

## 4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

## 4.5.1 CHRONIC TOXICITY TO FISH

## 4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

## 4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

## 4.6.2 TOXICITY TO TERRESTRIAL PLANTS

## 4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

## 4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

## 4.7 BIOLOGICAL EFFECTS MONITORING

## 4.8 BIOTRANSFORMATION AND KINETICS

## 4.9 ADDITIONAL REMARKS

## 5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

### 5.1.1 ACUTE ORAL TOXICITY

| | | |
|---|---|---|
| **Type** | : | LD50 |
| **Value** | : | = 3750 mg/kg bw |
| **Species** | : | mouse |
| **Strain** | : | other:albino |
| **Sex** | : | male |
| **Number of animals** | : | 39 |
| **Vehicle** | : | |
| **Doses** | : | 3.0, 4.0 and 5.0 ml/kg |
| **Method** | : | other |
| **Year** | : | 1953 |
| **GLP** | : | no |
| **Test substance** | : | as prescribed by 1.1 - 1.4 |
| **Result** | : | Very shortly after administration, squinting, lacrimation, rapid and labored respiration, ataxia and depression were noted, with vasodilation around the mouth, mild clonic convulsions and coma preceding death. Six animals treated with 3.38 mg/kg, seven treated with 4.44 mg/kg, and all animals treated with 5.55 mg/kg died during the study. All mid and high dose animals and 4/6 low dose animals that died succumbed within 24 hours. At 24 hours, some of the survivors were depressed but otherwise appeared normal.<br><br>Postmortem examinations of mice that died revealed hemorrhagic or hyperemic lungs, distended stomachs, irritated intestines (with vasodilation in some cases), mottled livers and granular kidneys. In addition, blood clots were observed in the region of the transverse sinuses of 2 mice treated with 4.4 g/kg. No other brain damage was observed grossly. Animals that survived until necropsy had normal gross pathology.<br><br>The LD50 values (with error limits) calculated for 48 hours and 10 days were 4.10 (2.73 - 6.15) and 3.75 (2.63 - 5.34) g/kg, respectively. The slopes of the curves for these time points were 1.361 and 2.217, respectively. |
| **Test condition** | : | Test material was administered by stomach tube at 3.0, 4.0 and 5.0 ml/kg to 3 groups of 13 rats each. Weights of the animals were not listed. Using a specific gravity of 1.1095, the values in g/kg were 3.38, 4.44 and 5.55. Animals were observed over a 10-day period for mortality or signs of toxicity. LD50 values at 48 hours and 10 days were calculated using the Wilcoxon and Litchfield method. |
| **Test substance** | : | The purity was listed as > = 90%. |
| **Reliability** | : | (1) valid without restriction<br>The study conduct was similar to a guideline study. |
| **Flag** | : | Critical study for SIDS endpoint |

(12)

### 5.1.2 ACUTE INHALATION TOXICITY

| | | |
|---|---|---|
| **Type** | : | LC50 |
| **Value** | : | > 15.5 ppm |
| **Species** | : | other: mouse, rat, guinea pig |
| **Strain** | : | |
| **Sex** | : | no data |

| | | |
|---|---|---|
| **Number of animals** | : | |
| **Vehicle** | : | |
| **Doses** | : | 15.5 ppm |
| **Exposure time** | : | 6 hour(s) |
| **Method** | : | other |
| **Year** | : | 1953 |
| **GLP** | : | no |
| **Test substance** | : | as prescribed by 1.1 - 1.4 |
| **Result** | : | The final concentration of test material in the chamber was 15.5 ppm. None of the animals died or exhibited signs of toxicity during exposure. After exposure, viscera were in their normal position and were normal in appearance and consistency. Vascular congestion was found throughout all tissues; however, since this also was found in normal controls, it was not due to treatment. There were no other significant microscopic findings. |
| **Test condition** | : | Seven mice (avg. wt. 30 g), 7 rats (avg. weight 297 g), 7 guinea pigs (avg. et. 457 g) were exposed in a 160 liter stainless steel chamber to a near-saturated vapor of test material for 6 hours. The air flow was maintained at 35 lpm. Vapor was generated by bubbling the air through the test material which was maintained at 36 degrees C. The concentration of test material in the chamber was determined by a modification of the Kjeldahl analysis for nitrogen. A known sample of the chamber atmosphere was drawn through 2 bubblers (in tandem) containing distilled water. An aliquot was analyzed for the total nitrogen content by the Kjeldahl method. Samples were also analyzed from chambers containing the same animals during exposure to air only to determine the background level of nitrogen. Known quantities of test material were also analyzed to determine the percent recovery of nitrogen from the test material. Animals were killed and examined grossly and microscopically after exposure. |
| **Test substance** | : | The purity was listed as > = 90%. |
| **Reliability** | : | (1) valid without restriction<br>The study conduct was similar to a guideline study. |
| **Flag** | : | Critical study for SIDS endpoint |

(13)

### 5.1.3 ACUTE DERMAL TOXICITY

| | | |
|---|---|---|
| **Type** | : | LD50 |
| **Value** | : | > 8 ml/kg bw |
| **Species** | : | rabbit |
| **Strain** | : | other: albino |
| **Sex** | : | no data |
| **Number of animals** | : | 9 |
| **Vehicle** | : | |
| **Doses** | : | 8.0 ml/kg |
| **Method** | : | other |
| **Year** | : | 1953 |
| **GLP** | : | no |
| **Test substance** | : | as prescribed by 1.1 - 1.4 |
| **Remark** | : | The cause of death in one high dose animal appeared to be a parasitic infection. |
| **Result** | : | None of the low or mid dose animals died before scheduled termination. Animals exposed to 1.0 ml/kg appeared depressed shortly after the material was applied but had normal behavior at 24 hours. There were no other signs of systemic toxicity or skin irritation, and weight gains were normal over the course of the study. Animals exposed to 4.0 ml/kg were observed to be hopping about in their cages shortly after application, which was indicative of burning or pain. Animals appeared normal within 24 hours. There were no other signs of toxicity in this group. Autopsies of low |

and mid-dose animals were normal.

One high dose animal died on the 4th day after application. This animal had experienced diarrhea (accompanied by weight loss) on day 2. At autopsy, this animal and another high dose animal that also experienced diarrhea and weight loss on day 2 but survived to study termination had a parasitic infestation of the liver, hyperemic lungs, and intestinal irritation. One of these animals also had mottled kidneys (it was not noted if this occurred in the animal that survived or in the one that died before scheduled termination). The third high dose animal also had diarrhea accompanied by weight loss on day 4, but did not have any significant findings upon gross necropsy.

The LD50 value was greater than the highest dose given (8.0 ml/kg). Based on a specific gravity of 1.1095, this value is 8.876 g/kg.

**Test condition** : Three groups of 3 albino rabbits (weights and sex were not indicated) received a single dermal application of undiluted test material at doses of 1.0, 4.0 and 8.0 ml/kg. The abdomens of low dose animals and the entire trunks of the mid and high dose animals were closely shaved prior to application of the test material. The material was applied under rubber damming. Mid and high dose animals were restrained in racks while the material was applied a little at a time to prevent leakage. Some loss from leakage was observed in the high dose group due to the large amount of material that was applied. The trunks of all animals were wrapped in gauze secured with adhesive tape to prevent ingestion. Dressings were removed after the material had been in contact with the skin for approximately 22 hours. Animals were then evaluated for dermal irritation and systemic toxicity. Additional observations were made daily thereafter for a period of 6-10 days. The animals were euthanized by air embolism and gross necropsies were performed.

**Test substance** : The purity was listed as > = 90%.

**Reliability** : (2) valid with restrictions
The results may have been influenced by the presence of a parasitic infection.

**Flag** : Critical study for SIDS endpoint

(12)

### 5.1.4 ACUTE TOXICITY, OTHER ROUTES

### 5.2.1 SKIN IRRITATION

| | | |
|---|---|---|
| **Species** | : | rabbit |
| **Concentration** | : | 1 other: ml/kg |
| **Exposure** | : | Occlusive |
| **Exposure time** | : | 10 day(s) |
| **Number of animals** | : | 6 |
| **Vehicle** | : | |
| **PDII** | : | |
| **Result** | : | |
| **Classification** | : | not irritating |
| **Method** | : | other |
| **Year** | : | 1953 |
| **GLP** | : | no data |
| **Test substance** | : | as prescribed by 1.1 - 1.4 |

**Result** : No skin irritation was noted after 10 days of application of the material.

**Test condition** : Six rabbits (sex and weight were not listed) were treated dermally on clipped abdominal skin with 1.0 ml/kg test material, 5 days/week, 22

hours/day, for a total of 10 applications. The material was applied under rubber damming and gauze binders were placed around the abdomens to hold the damming in place. Each day, after 22 hours of treatment, the dressings were removed and the animals were observed for systemic toxicity and skin irritation. Animals were then observed for toxicity for 10 additional days.

**Test substance** : The purity was listed as > = 90%.

**Reliability** : (2) valid with restrictions
The degree of irritation observed was not given a numerical score. However, since the material did not appear to cause irritation in any of the animals, this is not a serious drawback to the study.

(13)

### 5.2.2 EYE IRRITATION

| | | |
|---|---|---|
| **Species** | : | rabbit |
| **Concentration** | : | undiluted |
| **Dose** | : | .05 ml |
| **Exposure time** | : | |
| **Comment** | : | |
| **Number of animals** | : | 3 |
| **Vehicle** | : | |
| **Result** | : | slightly irritating |
| **Classification** | : | |
| **Method** | : | other |
| **Year** | : | 1953 |
| **GLP** | : | no |
| **Test substance** | : | as prescribed by 1.1 - 1.4 |

**Result** : Blinking and scrambling indicative of pain, vascularization of the sclera and nictitating membrane and some edema of the upper eyelid were noted immediately after application. A mild erythema also was observed in 2/3 rabbits. All eyes appeared normal after 1 hour. There was no evidence of systemic toxicity during the experiment.

**Test condition** : Test material (0.5 ml) was applied undiluted into the conjunctival sac of the left eye of each of 3 albino rabbits (weight and sex was not indicated). The eye was closed for approximately 30 seconds, after which an evaluation was taken. Additional observations were made 1, 4 and 24 hours after application, and daily thereafter for 1 week. The untreated right eyes served as controls. The animals were housed collectively.

**Test substance** : The purity was listed as > = 90%.

**Conclusion** : The authors concluded that the material caused "slight, transient irritation" during the first hour.

**Reliability** : (2) valid with restrictions
Fewer animals than recommended (6) were used. The effect of washing eyes after treatment was not assessed.

(12)

### 5.3 SENSITIZATION

| | | |
|---|---|---|
| **Type** | : | other |
| **Species** | : | rabbit |
| **Number of animals** | : | 6 |
| **Vehicle** | : | |
| **Result** | : | not sensitizing |
| **Classification** | : | |
| **Method** | : | other |
| **Year** | : | 1953 |

| | | |
|---|---|---|
| **GLP** | : | no |
| **Test substance** | : | as prescribed by 1.1 - 1.4 |
| **Result** | : | No skin irritation was noted after 10 days of application of the material or after application of the challenge dose. |
| **Test condition** | : | Six rabbits (sex and weight were not listed) were treated dermally on clipped abdominal skin with 1.0 ml/kg test material, 5 days/week, 22 hours/day, for a total of 10 applications. The material was applied under rubber damming and gauze binders were placed around the abdomens to hold the damming in place. Each day, after 22 hours of treatment, the dressings were removed and the animals were observed for sys temic toxicity and skin irritation. Animals were then observed for toxicity for 10 additional days. A challenge dose was then applied to determine if the material caused sensitization. |
| **Test substance** | : | The purity was listed as > = 90%. |
| **Reliability** | : | (4) not assignable<br>The study conduct is not up to current standards for sensitization studies. |

(13)

## 5.4 REPEATED DOSE TOXICITY

| | | |
|---|---|---|
| **Type** | : | Sub-chronic |
| **Species** | : | rat |
| **Sex** | : | male |
| **Strain** | : | other: Carworth Farms albino |
| **Route of admin.** | : | oral feed |
| **Exposure period** | : | 32 days |
| **Frequency of treatm.** | : | continuous |
| **Post exposure period** | : | |
| **Doses** | : | 100, 1,000, 10,000 ppm |
| **Control group** | : | yes |
| **Method** | : | other |
| **Year** | : | 1953 |
| **GLP** | : | no |
| **Test substance** | : | as prescribed by 1.1 - 1.4 |
| **Remark** | : | Based on the average amount of food consumed, the amount of test material consumed on a mg/day basis was 1.87, 18.23 and 169.31 mg/day for the 100, 1,000 and 10,000 ppm groups. Based on an average weight of 175.5, 174 and 167.5 g for rats treated with these concentrations (respect ively), the average amount of material consumed on a mg/kg/day basis was 10.7, 104.8 and 1010.8, respectively.<br><br>The authors concluded that there was no evidence of toxicity at any dose level. The authors apparently did not think that the deaths at 100 and 10,000 ppm or the gross pathological changes in the liver and kidneys at 1,000 and 10,000 ppm were related to administration of test material. However, there is no explanation for this conclusion. |
| **Result** | : | Overall: Average body weights of animals treated with 100, 1,000 or 10,000 ppm were not significantly different from controls at any time point. Food consumption for all groups was erratic, but within normal limits.<br><br>10,000 ppm: One rat exposed to 10,000 ppm died after 20 days on the study. This animal exhibited labored respiration, a bloody nose, an unthrifty appearance and a weight loss of 20 grams at the end of the second week. An autopsy was not performed on this animal due to advanced autolysis. All other animals survived to termination. At terminal autopsy, 1 animal in this group had a granular liver and mottled, muddy-colored kidneys. Another rat had muddy-colored kidneys. |

1,000 ppm: Two animals exhibited rough-surfaced kidneys upon terminal autopsy. One of these animals also had slight irritation of the intestines. A granular liver was noted in another rat treated with this dose.

100 ppm: One rat exposed to 100 ppm died after 17 days on the study. This animal exhibited an unthrifty appearance and a weight gain of 21 g at the end of the second week (average weight gain in the controls over 2 weeks was 51 g). An autopsy was not performed on this animal due to advanced autolysis. Gross pathology of animals surviving to necropsy was normal

**Test condition** : Four groups of 10 male rats each (100 - 130 g) were given 0, 100, 1,000 or 10,000 ppm of test material in the diet. They were individually housed and allowed free access to food and water. Body weight and food consumption were recorded weekly. Gross observations of the general appearance and behavior of each animal were made. The intervals at which these observations were made were not stated. All animals were euthanized after 32 days on the respective diets. At termination, 1 control and 3 animals from each of the other groups were killed by exsanguniation, gross autopsies were performed, and representative tissues (types were not stated except for the brain) were preserved for future histological examination. At the same time, one other control rat and the remaining experimental animals were killed by a blow on the head. Gross autopsies were performed on these animals, and representative tissues were preserved from the control animal only.

**Test substance** : The purity was listed as > = 90%.

**Reliability** : (4) not assignable
It is difficult to assign an NOAEL from this study. The conduct is not up to current standards. Organs were not examined histologically, and diets were not analytically tested for concentration of test material present, or stability or homogeneity of the test material. While the study does not appear to be invalid, it is not sufficient to fill the endpoint.

(13)

**Type** : Sub-acute
**Species** : Rabbit
**Sex** : no data
**Strain** : other:albino
**Route of admin.** : Dermal
**Exposure period** : 10 days
**Frequency of treatm.** : Daily
**Post exposure period** : 15 days
**Doses** : 1.0 ml/kg
**Control group** : no data specified
**NOAEL** : < 1 ml/kg bw
**Method** : other
**Year** : 1953
**GLP** : No
**Test substance** : as prescribed by 1.1 - 1.4

**Result** : None of the animals died. No skin irritation was noted after 10 days of application of the material or after application of the challenge dose. Five out of the 6 animals exhibited normal behavior and appearance and gained weight throughout the study. After 6 applications, one animal developed an apparent weakness or uncoordination of the hind extremities. This behavior persisted until study termination. Placement and righting reflexes in this animal were normal. This animal also developed diarrhea, weight loss, and an "unthrifty" appearance. There were no significant necropsy findings in any of the animals (including the animal with diarrhea).

**Test condition** : Six rabbits (sex and weight were not listed) were treated dermally on clipped abdominal skin with 1.0 ml/kg test material, 5 days/week, 22 hours/day, for a total of 10 applications. The material was applied under rubber damming and gauze binders were placed around the abdomens to

hold the damming in place. Each day, after 22 hours of treatment, the dressings were removed and the animals were observed for systemic toxicity and skin irritation. Animals were then observed for toxicity for 10 additional days. A challenge dose was then applied to determine if the material caused sensitization. The animals were euthanized 25 days after the first application and gross autopsies were performed. Tissues from representative were preserved (types were not stated) for future histologic examination. Animals were housed individually during the study and offered food and water ad lib.

**Test substance** : The purity was listed as > = 90%.

**Reliability** : (4) not assignable
This study has a reliability rating of 4 for repeated dose toxicity. It was not conducted similarly to current standards. Standard endpoints were not measured. Only one dose was tested.

(13)

## 5.5 GENETIC TOXICITY 'IN VITRO'

## 5.6 GENETIC TOXICITY 'IN VIVO'

## 5.7 CARCINOGENICITY

## 5.8.1 TOXICITY TO FERTILITY

## 5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

## 5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

## 5.9 SPECIFIC INVESTIGATIONS

## 5.10 EXPOSURE EXPERIENCE

## 5.11 ADDITIONAL REMARKS

## 6.1 ANALYTICAL METHODS

## 6.2 DETECTION AND IDENTIFICATION

## 7.1 FUNCTION

## 7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

## 7.3 ORGANISMS TO BE PROTECTED

## 7.4 USER

## 7.5 RESISTANCE

## 8.1 METHODS HANDLING AND STORING

## 8.2 FIRE GUIDANCE

## 8.3 EMERGENCY MEASURES

## 8.4 POSSIB. OF RENDERING SUBST. HARMLESS

## 8.5 WASTE MANAGEMENT

## 8.6 SIDE-EFFECTS DETECTION

## 8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

## 8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

(1) Cuthbert JE and Mullee DM. 2003. 3,3'-thiodipropionitrile (CT-781-03): Determination of melting point/melting range and hydrolysis as a function of pH. SafePharm Laboratories (SPL) project number 971/210, dated September 24, 2003 (unpublished).

(2) Cytec Industries, Inc. 1997. Material safety data sheet for thiodipropionitrile, dated July 1.

(3) EPIWIN AOP (v1.90)

(4) EPIWIN ECOSAR

(5) EPIWIN Fugacity Level III Model

(6) EPIWIN Kowwin (v1.66)

(7) EPIWIN Mpbpwin (v 1.40).

(8) EPIWIN Wskow (v1.40)

(9) RTECS.2003. Registry of toxic effects of chemical substances.

(10) The Dow Chemical Company. 2001. Material safety data sheet for thiodipropionitrile dated December 3.

(11) Tremain SP. 2003. 3,3'-thiodipropionitrile (CT-781-03): Determination of vapour pressure. SafePharm Laboratories (SPL) project number 971/211, dated September 24, 2003 (unpublished).

(12) Tusing TW. 1953. Progress Report : B,B' Thiodipropionitrile Acute Oral and Dermal Toxicity and Acute Eye Irritation. Hazleton Laboratories Report to American Cyanamid Company, dated Feb. 24, 1953.

(13) Tusing TW. 1953. Progress Report : B,B' Thiodipropionitrile Repeated Dermal Application, Acute Inhalation Toxicity, and Subacute Feeding. Hazleton Laboratories Report to American Cyanamid Company, dated March 30, 1953.

## 10.1 END POINT SUMMARY

## 10.2 HAZARD SUMMARY

## 10.3 RISK ASSESSMENT